

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
29 July 2004 (29.07.2004)

PCT

(10) International Publication Number
WO 2004/062606 A2

(51) International Patent Classification⁷: **A61K**

(21) International Application Number:
PCT/US2004/000541

(22) International Filing Date: 12 January 2004 (12.01.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/439,816 13 January 2003 (13.01.2003) US

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): HUMA-
NETICS CORPORATION [US/US]; 18894 Lake Drive
East, Chanhassen, MN 55317 (US).

(72) Inventor; and

(75) Inventor/Applicant (*for US only*): ZENK, John, L.
[US/US]; 4235 Trillium Lane East, Minnetrista, MN
55364 (US).

(74) Agents: SHERRILL, Michael, S. et al.; Sherrill Law Of-
fices, 4756 Banning Avenue, Suite 212, White Bear Lake,
MN 55110 (US).

Published:

— *without international search report and to be republished
upon receipt of that report*

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: METHOD OF ACHIEVING ACCELERATED FAT LOSS BY ADMINISTRATION OF A FAT LOSS ACCELERAT-
ING AGENT TO A DIETING MAMMAL

(57) Abstract: Accelerating fat loss by administering to a dieting mammal the fat loss accelerating agent 7-oxo DHEA or a pro-drug



O 2004/062606 A2

**METHOD OF ACHIEVING ACCELERATED FAT LOSS BY
ADMINISTRATION OF A FAT LOSS ACCELERATING AGENT TO A
DIETING MAMMAL**

[0001] This application claims the benefit of United States Provisional Application No. 60/439,816, filed January 13, 2003.

FIELD OF INVENTION

[0002] The invention relates to methods of achieving fat loss.

BACKGROUND

[0003] The steroid Δ^5 -androstene-3-ol-7,17-dione (7-oxo DHEA) is believed to stimulate various beneficial biological responses including (i) inducing the synthesis of various thermogenic enzymes which are effective for regulating metabolism and thereby promoting weight control without affecting caloric intake, and (ii) inducing the synthesis of the major thyroid hormone triiodothyronine (T_3) which is effective for increasing the basal metabolic rate and thereby promoting weight control without affecting caloric intake.

[0004] The ability of 7-oxo DHEA to promote weight control is widely believed to be mediated through enhanced thermogenesis (conversion of foodstuffs to heat energy rather than chemical energy such as ATP and/or triacylglycerides). The thermogenic effect mediated by 7-oxo DHEA is believed to result from the ability of 7-oxo DHEA to stimulate the synthesis of thermogenic enzymes including mitochondrial glycerol 3-phosphate dehydrogenase (G3P-DH), cytosolic malic enzyme (ME) and fatty acyl CoA oxidase. Such enzymes tend to reduce the efficiency of energy metabolism within the body.

[0005] While highly effective for safely promoting weight control, a continuing need exists for achieving accelerated fat loss.

SUMMARY OF THE INVENTION

[0006] Fat loss can be accelerated during dieting by the administration of a fat loss accelerating agent while dieting. The fat loss accelerating agent is 7-oxo DHEA or a pro-drug thereof incapable of in vivo conversion to testosterone.

DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

Definitions

[0007] As utilized herein, including the claims, the term "*dieting*" means eating and drinking sparingly with the intent to lose weight.

[0008] As utilized herein, including the claims, the term "*7-oxo DHEA*" means Δ^5 -androstene-3-ol-7,17-dione.

[0009] As utilized herein, including the claims, the term "*3-acetyl 7-oxo DHEA*" means Δ^5 -androstene-3-acetoxy-7,17-dione.

Description

[00010] I have surprisingly discovered that 7-oxo DHEA is effective for accelerating the loss of fat during dieting. Without intending to be limited to any particular theory, I believe that the administration of 7-oxo DHEA to a dieting mammal is effective for accelerating the loss of fat because 7-oxo DHEA modulates the metabolism of the dieting mammal. It is widely believed that dieting is an ineffective means for achieving fat loss because the body reacts to the reduced caloric intake by slowing down the metabolism of the dieter. By modulating the metabolism of the dieting mammal, 7-oxo DHEA would be effective for preventing or at least moderating any diet-induced decrease in the metabolism and thereby accelerate fat loss achievable by dieting.

The Fat Loss Accelerating Agent

[00011] The fat loss accelerating agent effective for accelerating the loss of fat when combined with dieting is the steroid Δ^5 -androstene-3 β -ol-7,17 dione (7-oxo DHEA). 7-oxo DHEA is a derivative of dehydroepiandrosterone (DHEA). 7-oxo DHEA does not appreciably stimulate, increase or otherwise enhance the production of sex hormones. The steroid is commercially available from a number of sources including Steraloids, Inc. of Wilton, New Hampshire. A number of procedures are available for synthesizing Δ^5 -androstene-3 β -ol-7,17 dione from DHEA, with one such procedure described in United States Patent No. 5,296,481.

[00012] Pro-drugs of 7-oxo DHEA (*i.e.*, compounds readily metabolized *in vivo* to the active 7-oxo DHEA) may also be usefully employed. One example of a pro-drug is the commercially available Δ^5 -androstene-3 β -acetyl-7,17 dione (3-acetyl 7-oxo DHEA). The 3 β -acetyl group is hydrolyzed *in vivo* by esterases located in the blood and various tissue to produce the active 7-oxo DHEA, and is believed to be less susceptible to oxidation during the manufacturing process relative to 7-oxo DHEA. Other suitable pro-drugs include Δ^5 -androstene-3 β , 17 β -diol-7-one, Δ^5 -androstene-3 β , 7 α -diol-17-one, Δ^5 -androstene-3 β , 7 β -diol-17-one and the corresponding acetyl esters of these steroids.

Administration

Administration Route

[00013] The fat loss accelerating agent can be administered by virtually any of the commonly accepted practices for the administration of pharmaceutical preparations including specifically, but not exclusively, mucosal administration, oral consumption, ocular administration, subcutaneous injection, transdermal administration, etc. Oral administration is generally preferred.

[00014] Mucosal administration of the fat loss accelerating agent includes such routes as buccal, endotracheal, nasal, pharyngeal, rectal, sublingual, vaginal, etc. For administration through the buccal/sublingual/pharyngeal/endotracheal mucosal, the fat loss accelerating

agent may be formulated as an emulsion, gum, lozenge, spray, tablet or an inclusion complex such as cyclodextrin inclusion complexes. Nasal administration is conveniently conducted through the use of a sniffing powder or nasal spray. For rectal and vaginal administration the fat loss accelerating agent may be formulated as a cream, douche, enema or suppository.

[00015] Oral consumption of the fat loss accelerating agent may be effected by incorporating the fat loss accelerating agent into a food or drink, or formulating the fat loss accelerating agent into a chewable or swallowable tablet or capsule.

[00016] Ocular administration may be effected by incorporating the fat loss accelerating agent into a solution or suspension adapted for ocular application such as drops or sprays.

[00017] Subcutaneous administration involves incorporating the fat loss accelerating agent into a pharmaceutically acceptable and injectable carrier.

[00018] For transdermal administration, the fat loss accelerating agent may be conveniently incorporated into a lipophilic carrier and formulated as a topical crème or adhesive patch.

Dose Rate

[00019] The range of dosages and dose rates effective for achieving the desired accelerative fat loss effect may be determined in accordance with standard industry practices.

I/we claim:

1. A method of achieving accelerated fat loss comprising administration of a fat loss accelerating agent to a dieting mammal wherein the fat loss accelerating agent is 7-oxo DHEA or a pro-drug thereof incapable of in vivo conversion to testosterone.
2. The method of claim 1 wherein the fat loss accelerating agent is administered orally.
3. The method of claim 2 wherein the fat loss accelerating agent is administered at least once daily.
4. The method of claim 1 wherein the dieting mammal is a human.
5. The method of claim 2 wherein the dieting mammal is a human.
6. The method of claim 3 wherein the dieting mammal is a human.
7. The method of claim 4 wherein the fat loss accelerating agent is 3-acetyl 7-oxo DHEA or 3-ester thereof.
8. The method of claim 5 wherein the fat loss accelerating agent is 3-acetyl 7-oxo DHEA or 3-ester thereof.
9. The method of claim 6 wherein the fat loss accelerating agent is 3-acetyl 7-oxo DHEA or 3-ester thereof.